Remarks

The July 8, 2005 Requirement for Restriction issued in the above-identified patent application has been carefully reviewed. The Examiner contends that the originally filed claims are directed to twenty (20) distinct inventions. These are as follows:

Group I: Claims 1-39 drawn to methods for screening for agents for treating pancreatic islet or beta cell dysfunction;
Group II: Claims 44-45 and 50 drawn to methods of treating pancreatic islet or beta cell dysfunction;
Group III: Claims 46-49 drawn to methods of determining the nature/degree of pancreatic islet or beta cell dysfunction;
Group IV: Claims 51-52 drawn to a method used to select an appropriate therapy for pancreatic islet or beta cell dysfunction; and
Group V: Claims 53-56 drawn to proteins.

It is the Examiner's position that the inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1, because, under PCT Rule 13.2, they lack the same or corresponding special technical feature. In the event, Applicant chooses to elect the Group V invention, the Examiner requires further election of one of the 15 POM proteins encompassed by the claim asserting each of these comprises a patentably distinct invention.

Finally, the Examiner has determined that each of the recited proteins in the Markush group of claim 57 comprises a patentably distinct invention which are set forth as Groups VI-XX in the restriction requirement. Applicants strenuously disagree with the Examiner's position in this regard for the reason set forth below.

Applicants respectfully assert that the restriction requirement set forth above is improper for failure to comply

with the relevant provisions of the Manual of Patent Examining Procedure (M.P.E.P.) pertaining to unity of invention determinations.

The present application was filed under 35 U.S.C. §371 as a U.S. national stage application under the Patent Cooperation Treaty.

As stated in § 1893.03(d) of the M.P.E.P.:

> Examiners are reminded that unity of invention (not restriction) practice is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. § 371...
>
> The principles of unity of invention are used to determine the types of claimed subject matter and the combinations of claims to different categories of invention that are permitted to be included in a single international or national stage patent application. The basic principle is that an application should relate to only one invention or, if there is more than one invention, that applicant would have a right to include in a single application only those inventions which are so linked as to form a single general inventive concept.
>
> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art....

It is the Examiner's position that the inventions listed as Groups I-XX do not relate to a single general inventive concept under PCT Rule 13.1, because, under PCT Rule 13.2, they lack the same or corresponding special technical feature. The Examiner has also declined to search the claims which were not searched by the IPEA.

The requirements of the PCT are, of course, supposed to take precedence over normal national practice for the national phase of a PCT application. In particular, it is not permissible under the PCT for national offices to require compliance with the requirements relating to the form or contents of the application different from or additional to

those which are provided for in the PCT (Art 27 PCT). In this specific instance, the PCT Handbook says at section 33.35, paragraph 2 "a designated office ought not to raise an objection as to a lack of unity when the International Searching and/or Preliminary Examining Authority has found that the claims comply with the requirement for unity of invention". Indeed, the PCT Contracting States have agreed to this principle, according to the PCT Handbook at Section 23.9 paragraph 2 (which refers to the report of the PCT assembly, 18th session (1991), item 24).

Notably, during the international stage of this application, the Examiner **did not** make a lack of unity finding and considered all of the claims to be directed to a single invention.

Plainly, the written restriction requirement fails to comply with the established United States Patent and Trademark Office practice of following the international rules regarding unity of invention in the prosecution of applications filed under § 371. It is unclear how the Examiner could conclude that instant application now has twenty Groups of inventions, when the international application from which it originates has unity of invention.

The claims have been amended to more clearly set forth the subject matter regarded as the invention. The presently claimed drug screening methods are used to assess the efficacy of agents useful for modulating insulin sensitivity in test subjects having reduced or increased pancreatic islet or β cell function. The method is performed by first identifying those proteins which are differentially expressed in subjects having reduced or increased pancreatic islet or β-cell function and normal subjects, the samples being obtained before and after treatment of said subjects with a compound which alleviates or improves pancreatic islet or β-cell dysfunction. An insulin responsive tissue or subcellular fraction thereof is then contacted with the test agent, and

the ability of the agent to modulate differential protein expression in the tissue is assessed. These results are then compared to those obtained from the subjects having reduced or increased pancreatic islet or β-cell function before and after treatment of said subjects with a compound which alleviates or improves pancreatic islet or β-cell dysfunction thereby identifying test agents which modulate protein expression levels towards that of a of subject having substantially normal pancreatic islet or β cell function. Because the expression pattern obtained in response to the test agent is compared to that obtained in response to known treatments, the skilled person can more accurately identify those agents which should have efficacy for the treatment of disorders relating to pancreatic islet or β cell dysfunction. Claim 1 has been amended to clarify the method being claimed. Support for the amendments to claim 1 can be found in original claims 8-13 and at page 26, line 16 to page 27, line 19. Support for the recitation of the sample in step b) comprising "tissue or cells that undergo a biological change in response to insulin can be found at page 17, lines 15-20. It is respectfully submitted that the subject matter of claim 1 and the amendments thereto are fully supported by the disclosure in the application as filed and are clearly encompassed within the Group I invention.

An important feature of the instantly claimed method is the comparison step of proteins which are already known to possess altered expression levels in response to previously identified treatments which modulate pancreatic islet or β cell function in different test subjects and the expression levels of proteins which are altered in response to contact with the test agent. Comparing the populations of differentially expressed proteins enables the skilled person to identify agents which create more desirable protein expression patterns, i.e., those of a subject having normal

pancreatic islet or beta cell function. Thus, it is Applicants position that any protein which exhibits the foregoing characteristics is encompassed by the claim, thus, the election of a single protein from claim 57 is onerous and unwarranted. It appears as if the Examiner is treating claim 57 as a composition of matter claim, whereas the claim merely recites different proteins identified in the presently disclosed methods. It is respectfully requested that the Examiner re-consider this requirement for restriction should the subject matter of claim 1 be found allowable over the prior art.

Finally, according to the MPEP §803.01, there are two criteria for restriction between inventions which are alleged to be patentably distinct: 1) the inventions must be independent and distinct as claimed and 2) there must be a serious burden on the Examiner if the restriction is not required.

Notably, claims 44, 45, 47 and 48 depend directly or indirectly from claim 1. Accordingly, it cannot be reasonably maintained that the invention encompassed by these claims is "independent as claimed". Thus, it is respectfully requested that these claims be rejoined with the Group I invention, namely claims 1-39.

In order to be fully responsive, Applicants hereby elect the claims of the Group I invention for prosecution at this time.

Applicants reserve the right to file one or more continuing applications under 35 U.S.C. §120 on the subject matter of any claims finally held withdrawn from consideration in this application.

Favorable consideration leading to prompt allowance of the present application is respectfully requested.

Respectfully submitted,
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